

### **REMARKS**

Claims 1-4, 24-56 and 108-118 are pending. No claim has been amended or canceled. No new claims have been added.

#### **Rejections Under 35 U.S.C. § 112, Second Paragraph**

The Examiner rejected claims 27-29, 32-34, 38-40, 43-45, 49-51, and 54-56 for allegedly having insufficient antecedent basis in the base claim for the limitations “halophenyl” and “3-chlorophenyl.” The Applicants respectfully traverse.

The Applicants respectfully contend that claims 27-29, 32-34, 38-40, 43-45, 49-51, and 54-56 comply with the requirements of 35 U.S.C. § 112, second paragraph, because they are reasonably definite, even if they are not as definite as the Examiner prefers. *MPEP* 2173.02 (“The examiner's focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. § 112, second paragraph, is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. When the examiner is satisfied that patentable subject matter is disclosed, and it is apparent to the examiner that the claims are directed to such patentable subject matter, he or she should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire.”).

Moreover, the Applicants respectfully contend that the base claim does have sufficient antecedent basis for the cited claim limitations. In the instant case, the term “aryl” is defined in Column 3, Paragraph [0036] of the specification as “5-, 6-, and 7-membered single-ring aromatic groups that may include from 0 to 4 heteroatoms, for example, benzene, ...” One skilled in the art would readily understand that phenyl is the conventional aryl group counterpart to benzene. For example, chlorobenzene is also commonly called phenyl chloride. Furthermore, the specification states in Column 3, Paragraph [0036] that “the aromatic rings can be substituted at one or more ring positions with such substituents as described above, for example, halogen.” And, in Column 3, Paragraph [0039] “halogen” is defined as including “-F, -Cl, -Br, or -I.”

Thus, both “halophenyl” and “3-chlorophenyl” have sufficient antecedent basis in the base claim, wherein R<sup>3</sup> can be “aryl.” Additionally, as presented in Column 2, Paragraph [0026] of the specification, “the piperidine ring may be substituted at the 4-position ... with an optionally substituted phenyl group,” and “in a preferred embodiment, “the piperidine ring is substituted at the 4-position with 3-chlorophenyl.” Thus, it would be clear to one of ordinary skill that “aryl”, as used in the base claim, is inclusive of “substituted phenyl,” generally; and “halophenyl” and “3-chlorophenyl,” specifically.

Based on the foregoing, the Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

#### **Rejections Under 35 U.S.C. § 103(a)**

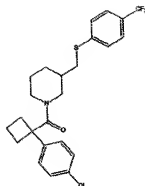
The Examiner rejected claims 1-4, 24-29, 32, 35-40, 43, 46-51, 54, 108-113, and 116 under 35 U.S.C. § 103(a) as being unpatentable over Aquila et al. (US 7,517,892; “the ‘892 patent”). The Applicants respectfully traverse.

#### **Legal Standard**

To establish a *prima facie* case of obviousness, a number of criteria must be met. For example, all of the limitations of a rejected claim must be taught or suggested in the references relied upon by the Examiner; or they must be among the variations that would have been “obvious to try” to one of ordinary skill in the relevant art in light of the cited references. Moreover, one of ordinary skill in the relevant art must have a reasonable expectation of success in light of the combination of cited references. Importantly, the reasonable expectation of success must be found in the prior art, and may not be based on the Applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991); see MPEP § 2143 - § 2143.03 for decisions pertinent to each of these criteria.

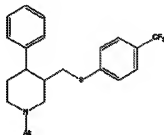
#### **Scope of the ‘892 Patent**

The Examiner points out that “Aquila et al. ‘892 disclosed examples 41-42 which” disclose the structure reproduced below. The Applicants agree.



*Compound in Examples 41-42 of the '892 patent*

However, the Examiner also contended that in the '892 patent "the exemplified species corresponding to the generic disclosure when R3 is H, R4 is cycloalkyl, R5, R6 forms a CO (see col. 12-13 formula A). Generically, the R3 moiety is optionally aryl (col. 13, lines 6-7), and R4, R5, R6 can all be H or alkyl (coll. 13, lines 10-15)." Based on the cited excerpts of the '892 patent the Examiner contended that the compound disclosed in Examples 41-42 "is tantamount to" the generic compound reproduced below.

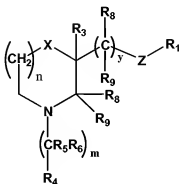


*Examiner's proposed generic compound from the '892 patent*

The '892 patent does not teach or disclose any compounds which are substituted with "H, alkyl, aryl, aralkyl or  $-C(O)R^5$ " at the nitrogen of the piperidine ring. In fact, Aquila et al. discloses over 200 compounds that contain other varieties of substituents, such as 1-(1-(4-(trifluoromethyl)phenyl)cyclobutyl)ethanone, attached to the N of the piperidine ring. In addition, the numerous compounds taught in Aquila et al. are not substituted in the 4-position of the piperidine ring (the position at which R<sub>3</sub> resides in formulas I-IV of the instant claims).

The Applicants respectfully disagree with the Examiner's interpretation of the disclosure of the '892 patent and her conclusions. The Applicants contend that the Examiner may not base

an obviousness rejection on an undisclosed generic compound that reflects arbitrary selection and combination of individual identities of numerous independent variables presented in the cited art. The generic structure at column 12, ll. 45-55, of the '892 patent is reproduced below.



A

The process of selecting and experimentally validating specific subgenuses and species within the generic structure from the '892 patent is just the sort of inventive effort that the patent system is designed to encourage, and that should be rewarded with a patent. In fact, Applicants submit that without the benefit of Applicants' invention as a road map one of ordinary skill in the art would not have arrived at the claimed invention. Moreover, the Federal Circuit has held that "in cases involving new compositions of matter, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound." *Takeda v. Alphapharm*, 492 F.3d 1350 (Fed. Cir. 2007).

#### All of the Claim Limitations

The Applicants respectfully contend that the Examiner has failed to establish a *prima facie* case of obviousness of the rejected claims because the '892 patent doesn't teach all of the limitations of the rejected claims.

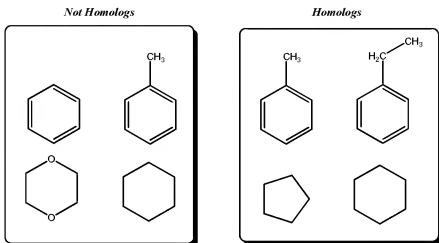
The Applicants claim compounds of formula I-IV in the instant application, where formulas I-IV are related as stereoisomers. In the interest of simplifying the discussion, below is a representative structure, formula I.



First, all of the limitations in the instant claims are not taught or suggested by the cited reference, nor would they be obvious to try to one of ordinary skill. The first limitation that is not taught or suggested by the cited reference is that “m” must be equal to “1, 2, 3, or 4” in the rejected claims. In *Aquila et al.*, m is 0. The second limitation that is not taught or suggested by the cited reference is that R<sub>3</sub> is “aryl, heteroaryl, or aralkyl” in the rejected claims. In the compounds of Examples 41-42 of *Aquila et al.*, R<sub>3</sub> is hydrogen.

The Applicants concede that homology and isomerism are facts which must be considered with all other facts in determining obviousness. MPEP § 2144.09. Nevertheless, although homology and isomerism involve close structural similarity, they must be considered with all other relevant facts in determining the issue of obviousness. *In re Mills*, 281 F.2d 218, 126 USPQ 513 (CCPA 1960); *In re Wiechert*, 370 F.2d 927, 152 USPQ 247 (CCPA 1967). Critically, homology should not be automatically equated with *prima facie* obviousness because the claimed invention and the prior art must each be viewed “as a whole.” *In re Langer*, 465 F.2d 896, 175 USPQ 169 (CCPA 1972) (Claims to a polymerization process using a sterically hindered amine were held unobvious over a similar prior art process because the prior art disclosed a large number of unhindered amines and only one sterically hindered amine (which differed from a claimed amine by 3 carbon atoms), and therefore the reference as a whole did not apprise the ordinary artisan of the significance of hindered amines as a class.)). Further, the Examiner has based some of reasoning on an incorrect interpretation of the concept of homology. While it is true that methyl, ethyl and propyl moieties, which differ from one another solely in the number of methylene units, are homologs, it does not follow that all compounds which differ by the number of methylene units are homologs. Examples of such compounds that are not homologs are depicted below, including pairs of compounds in which one of them has zero methylene units and the other compound has one or more methylene units. This distinction

is particularly important here because in the rejected claims *m* is 1, 2, 3, or 4; whereas, in the compound in Examples 41-42 of the '892 patent there is no methylene unit (i.e., *m* would be 0) between the sulfur atom and 4-chlorophenyl moiety in the side chain.



*Obvious to Try*

The Applicants respectfully contend that the differences between the claimed subject matter and the disclosure of the '892 patent are beyond what the Examiner may characterize as obvious to try.

A rationale to support a conclusion that a claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art. See MPEP 2143.02; *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385, 1395 (2007); *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); *Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp.*, 340 U.S. 147, 152, 87 USPQ 303, 306 (1950). Further, whether an art is predictable or whether the proposed modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. *Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986).

Here, the Applicants submit that the differences between the claimed subject matter and the disclosure of the '892 patent are not obvious to try because: (i) the rejected claims are tailored to a specific subgenus of compounds discovered by the Applicants to be particularly suitable for the described and enabled therapeutic utilities; and (ii) the rejected claims reflect specific combinations of structural features, substituents, and charge that were not suggested by the teachings of Aquila et al. The mere fact that one could explore and vary a number of possible variables to arrive at the claimed subject matter does not establish obviousness because there would have been no reasonable expectation that the claimed compounds would be preferred over any others within the genus disclosed by Aquila et al. *Takeda v. Alphapharm*, 492 F.3d 1350 (Fed. Cir. 2007) ("in cases involving new compositions of matter, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound.").

*No Reasonable Expectation of Success*

The Applicants respectfully contend that one of ordinary skill would not have had a reasonable expectation of success in developing the claimed subject matter based on the '892 patent. The development of pharmaceuticals is well understood to be an "unpredictable art." *See Eisai*, 533 F.3d 1353, 1359 (quoting *KSR*, 127 S. Ct. at 1742). The reference cited by the Examiner does not teach or disclose any compounds which are substituted with "H, alkyl, aryl, aralkyl or -C(O)R<sup>5</sup>" at the nitrogen of the piperidine ring. In fact, Aquila et al. discloses over 200 compounds that contain other varieties of substituents, such as 1-(1-(4-(trifluoromethyl)phenyl)cyclobutyl)ethanone, attached to the N of the piperidine ring. In addition, the numerous compounds taught, and claimed, in Aquila et al. are not substituted in the 4-position of the piperidine ring (the position at which R<sub>3</sub> resides in formulas I-IV). In the rejected claims R<sub>3</sub> is "aryl, heteroaryl, or aralkyl." Thus, the compounds found in the prior art are both sterically and electronically distinct from the claimed compounds. Furthermore, the compounds disclosed by Aquila et al. which possess any reported utility – as therapeutic compounds – all have m = 0; hydrogen at the position corresponding to R<sub>3</sub>, and substituents (such as 1-(1-(4-(trifluoromethyl)phenyl)cyclobutyl)ethanone) at R<sub>2</sub>. Based on the structure-activity information taught or suggested by Aquila et al. there could have been no reasonable

expectation that the instantly claimed compounds would have any activity, since one of ordinary skill in the art would appreciate that even slight differences in sterics or hydrophobicity can dramatically affect the activity of a compound.

The process of selecting and experimentally validating specific subgenres and species within the generic structure from the '892 patent is just the sort of inventive effort that the patent system is designed to encourage, and that should be rewarded with a patent. In fact, Applicants submit that without the benefit of Applicants' invention as a road map one of ordinary skill in the art would not have arrived at the claimed invention. Moreover, the Federal Circuit has held that "in cases involving new compositions of matter, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound." *Takeda v. Alphapharm*, 492 F.3d 1350 (Fed. Cir. 2007).

Based on the foregoing, the Applicants respectfully request reconsideration and withdrawal of the rejection under 35 USC § 103(a).

**Objections Based On Dependence Upon A Rejected Base Claim**

Claims 30-31, 33-34, 41-42, 44-45, 52, 55-56, 114-115, 117 and 118 are objected to by the Examiner based on their dependence upon a rejected base claim. Applicants gratefully acknowledge the Examiner's indication that the subject matter of the objected claims is novel and nonobvious in light of the art of record. However, the claims have not been amended in this paper because Applicants respectfully contend that the objections are moot in light of the foregoing arguments. Therefore, Applicants respectfully request withdrawal of the objections.



**FEES**

The Applicants believe that they have provided for all of the required fees in connection with the filing of this Response. Nevertheless, the Commissioner is hereby authorized to charge any additional required fees to our Deposit Account, No. 06-1448 reference GUX-010.01.

**CONCLUSION**

In view of the above remarks, it is believed that the pending claims are in condition for allowance. The Applicants respectfully request reconsideration and withdrawal of the pending rejections. The Applicants thank the Examiner for careful consideration of the present case. If a telephone conversation with the Applicants' Attorney would expedite prosecution of the above-identified application, the Examiner is urged to contact the undersigned.

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Respectfully submitted,

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